REMARKS

Claims 1 - 6 and 11 – 14 have been withdrawn. Claims 9 – 10 have been canceled. Claims 7 - 8 have been amended, are pending and are the subject of this Office Action. Support for claims 7 - 8 can be found throughout the specification including the Drawings and claims as filed originally. No new matter has been added.

Applicant respectfully reserve the right to pursue any non-elected, withdrawn, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

It is submitted that the claims, herewith and as originally presented were in full compliance with the requirements of 35 U.S.C. § 112. The amendment of the claims, as presented herein, is not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, this amendment is made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendment should not give rise to any estoppel.

Reconsideration and withdrawal of the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

Applicant now turns to comments made by the Examiner in this Office Action as follows.

Office Action

1. The rejection of claims 7-10, are rejected under 35 U.S.C. 103(a) as being unpatentable over Kosaka et al. (Exp Cell Res 245: 245-251, 1998) in view of Haruta et al., (Nat Neurosc 4: 1163-1164, 2001), is applied to the amended claims 7-8, for reasons of record in the Office Action, dated 8 January 2009.

> The Examiner states, "Applicant's arguments are based on the current claim amendments. Specifically Applicant argues that the

present invention as recited in amended claim 7 is drawn to the use of iris pigmented epithelial cells "not being subjected to a gene transfer", while the Haruta reference teaches differentiation into retinal nerve cells after a "Crx gene is transferred and forcibly expressed" in the iris-derived cells. Applicant also argues that Haruta teaches iris derived cells that are different from the claimed iris pigmented epithelial cells, because the cells of Haruta do not produce retinal photoreceptor cell marker rhodopsin, without the Crx gene transfer. Applicant concludes that the invention as currently amended in claim 7 is non-obvious over the prior art teachings because the skilled person would not accomplish the same results as claimed, without forcibly expressing the Crx gene in the iris-derived cells. As such the rejection is requested to be withdrawn.

Applicant's arguments are fully considered but not found to be persuasive, because arguments that rely on particular distinguishing features are not persuasive when those features are not recited in the claims. Applicant's arguments are largely directed to the Haruta reference, emphasizing the limitations inserted in the current claim amendments. As stated in the previous Office Action, Haruta et al teach the plating and maintenance of iris tissue from adult rats in serum free culture medium containing bFGF or FGF2, resulting in the proliferation of cells as a monolayer (Figure 1a, page 1163, para 2). Haruta et al. also teach that the iris derived cells are positive for a retinal ganglion cell marker, neurofilament 200, wherein such differentiation into a retinal nerve cell is accomplished without any gene transfer. The previous Office Action does not describe Figures 2 or 3, nor does it describe the differentiation to retinal photoreceptor cells from iris derived cells by transferring a Crx gene, as extensively argued by Applicant. Furthermore, the claims as amended do not require the differentiation to retinal photoreceptor cells, **nor do they specifically recite that the retinal nerve cells are photoreceptor cells that produce rhodopsin.** Therefore, Applicant is diverting the arguments to the newly amended subject matter, side-tracking the arguments presented in the previous Office Action.

The instant claims require a method for producing retinal nerve cells by isolating and differentiating iris pigmented epithelial cells, wherein the differentiation is induced by adherent culturing in a serum-free culture medium containing one of FGF2, FGF9 and CNTF. Based on the definition provided in the instant disclosure, a nerve cell can comprise neurons as well as non-neuronal or glial cells (para 0122, 0123), and a retinal nerve cell can comprise a retinal visual cell, bipolar cell, Muller glial cells, etc. (para 0040). Additionally iris-derived cells are broadly defined as comprising IPE cells, and Kosaka et al teach the isolation of IPE cells. It is to be noted that USPTO personnel are to give claims their broadest reasonable

> interpretation in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). Narrow limitation contained in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. See In re Philips Industries, Inc. v. State Stove & Mfg. Co., 522 F.2d 1137, 186 USPQ 458 (CA6 1975), 237 PTJA A-12. While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See Ex parte Oetiker, 23 USPQ2d 1641 (BPAI, 1992). Applicant is reminded that the claims define the subject matter of his invention and that the specification cannot be relied upon to read limitations into the claims.
>
> In view of the above discussion, it is reiterated from the last Office Action that:
>
> It would have been, therefore, obvious to the person of ordinary skill in the art at the time the claimed invention was made to modify the method of inducing differentiation of IPE cells to lens cells by adherent or monolayer culture method in medium containing serum as taught by Kosaka et al., to the monolayer culture in a serum free medium of Haruta et al., whereby the iris derived cells differentiate to retinal cells expressing neuronal antigen (i.e. inherently retinal nerve cells). The person of ordinary skill in the art would have been motivated because IPE and the neural retina have a common developmental origin, thereby giving rise to retinal neurons (Haruta et al. page 2163).
>
> Because, the source of the cells and culture conditions in the prior art teachings and the currently claimed invention are the same, the claimed invention as a whole stands *prima facie* obvious over the combined teachings of the prior art and stay rejected."

Applicants respectfully disagree. The Examiner alleges that the Haruta reference teaches that the iris derived cells are positive for a retinal ganglion cell marker, neurofilament 200, wherein such differentiation into a retinal nerve cell is accomplished without any gene transfer.

However, also Haruta does not teach that the cells express rhodopsin, a marker for rod photoreceptors. Claim 7 has been amended to limit the retinal nerve cells to "rhodopsin-positive" retinal nerve cells.

In view of the above, Applicant respectfully considers that Haruta et al. does not teaches iris derived cells are differentiated into rhodopsin-positive retinal nerve cells without any gene transfer.

The Examiner alleges that a person of ordinary skill in the art would have been motivated to differentiate iris pigmented epithelial cells (IPE cells) into retinal nerve cells because IPE cells and the neural retina have a common developmental origin, thereby giving rise to retinal neurons. However, at the time of filing of the present application, it was completely unknown whether IPE cells can be differentiated into retinal nerve cells regardless of the fact that IPE cells and retinal nerve cells have a common developmental originand, in particular, rhodopsin-positive retinal nerve cells. "*Biochem. Biophys. Res. Commun.*, 2004 March 26; 316(1), pgs. 1-5", a treatise written by the inventors of the present invention, reports the result of examining differentiation from human retinal pigment epithelial cells to neurons (this treatise is attached hereto). The treatise describes that although retinal pigment epithelial cells could be induced into neuron-like cells, it was difficult to induce the retinal pigment epithelial cells into particular retinal cells, and no cells positive for a photoreceptor cell marker was observed. The cells of the present invention, as now amended in claim 7, express rhodopsin, a marker for rod photoreceptors.

Applicant, in particular, believes that a conclusion of obviousness cannot be made in view of the U.S. Supreme Court's and the USPTO's current interpretation of obviousness under 35 U.S.C. § 103.

The PTO has issued Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 ("Guidelines") in view of the Supreme Court's recent decision in KSR International Co. v. Teleflex Inc., 550 U.S. __, 82 USPQ2d 1385 (2007). The Guidelines were published in the Fed. Reg., Vol. 72, no. 195, October 10, 2007. As pointed out in the Guidelines, the Supreme Court in KSR reaffirmed the analytical framework for determining obviousness as set forth in Graham v. John Deere Co., 338 U.S. 1, 148 USPQ 459 (1966), and also held that the Federal Circuit's application of its teaching-suggestion-motivation test was too formalistic.

Under Graham, obviousness is a question of law based on underlying factual inquiries that address (1) the scope and content of the prior art, (2) the differences between the claimed invention, and (3) resolving the level of ordinary skill in the pertinent art. Consideration must also be given to secondary factors, such as, for example, evidence of commercial success, long felt but unsolved needs, failure of others, and unexpected results. The Supreme Court stated in KSR that "While the sequence of these questions might be reordered in any particular case, the [Graham] factors continue to define the inquiry that controls." The Guidelines go on to state that "Once the *Graham* factual inquiries are resolved, Office personnel must determine whether the claimed invention would have been obvious to one or ordinary skill in the art."

The Guidelines proceed then to articulate seven independent rationales on which to properly base a rejection under 35 U.S.C. § 103: (1) combining prior art elements according to known methods to yield **predictable results**, (2) substitution of one known element for another to obtain **predictable results**, (3) use of known technique to improve similar devices, methods or products in the same way, i.e., to obtain **predictable results**, (4) applying a known technique to a known device, method or product ready for improvement to yield **predictable results**, (5) choosing from a finite number of identified, **predictable solutions**, with a reasonable expectation of success, i.e., obvious to try, (6) evidence of design incentives or other market forces sufficient to prompt skilled artisan to vary prior art in a **predictable manner** to result in claimed invention, and (7) evidence of some teaching, suggestion, or motivation in the prior art that would have led the skilled artisan to modify or combine prior art to arrive at claimed invention, i.e., **predictable** modification. All of these tests have the requirement of **predictability**. That is lacking in the present case.

In view of the above, at the time of filing of the present application, a person of ordinary skill in the art could not **predict** that IPE cells can be differentiated into rhodopsin-positive retinal nerve cells although IPE cells and retinal nerve cells have a common development origin. Accordingly, Applicant respectfully considers that a

person of ordinary skill in the art would not have been motivated to differentiate IPE cells into rhodoposin-positive retinal nerve cells.

Therefore, claim 7 directed to differentiation from IPE cells into rhodopsin-positive retinal nerve cells is not obvious over Kosaka in view of Haruta. Consequently, claim 8 depending from claim 7 is not obvious over Kosaka in view of Haruta.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

CONCLUSION

Applicants submit that all claims are allowable as amended and respectfully request early favorable action by the Examiner. Applicant's representative would like to discuss this case with the Examiner to learn if any outstanding issues remain after consideration of this Amendment. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record. Although it is not believed that any further fee is needed to consider this submission, the Office is hereby authorized to charge our deposit account **04-1105** should such fee be deemed necessary.

Dated: November 12, 2009

Respectfully submitted,

By _____

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